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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,061	08/31/2001	Jean-Yves Bonnefoy	PF86PCTSEQ	1138

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,061	BONNEFOY ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,27,28,31 and 35-48* is/are pending in the application.

4a) Of the above claim(s) *40-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25, 27, 28, 31 and 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

REQUEST FOR CONTINUED EXAMINATION

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 03/11/05 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 01/11/05 in response to the final Office Action mailed 09/08/04.

Status of Claims

3) Claims 25, 38 and 39 have been amended via the amendment filed 01/11/05.

Claims 25, 27, 28, 31 and 35-48 are pending.

Claims 25, 27, 28, 31 and 35-39 are under examination.

Objection(s) Maintained

4) The objection to the specification made in paragraph 8 of the Office Action mailed 08/29/03 and maintained in paragraph 6 of the Office Action mailed 09/08/04 is maintained for reasons set forth therein.

Rejection(s) Withdrawn

5) The rejection of claim 25 made in paragraph 27(a) of the Office Action mailed 09/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

6) The rejection of claims 38 and 39 made in paragraph 27(b) of the Office Action mailed 09/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

7) The rejection of claims 27, 28, 31 and 35-39 made in paragraph 27(c) of the Office Action mailed 09/08/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

8) The rejection of claims 25, 27, 28, 31 and 35-39 made in paragraph 28 of the Office Action

mailed 09/08/04 under 35 U.S.C. § 102(a) as being anticipated by Andreoni *et al.* (WO 99/49892A2, already of record; English translation provided), is withdrawn in light of Applicants' amendment to the base claim. Applicants' arguments with regard to this rejection have been considered, but are moot in light of the withdrawal of the rejection and/or the new ground of rejection made below.

9) The rejection of claims 25, 27, 28, 31, 35, 36 and 39 made in paragraph 29 of the Office Action mailed 09/08/04 under 35 U.S.C. § 102(b) as being anticipated by Binz *et al.* (WO 97/41888-A1, already of record - English translation provided) as evidenced by Pease *et al.* (US 2004/0014207 A1), is withdrawn in light of Applicants' amendment to the base claim. Applicants' arguments with regard to this rejection have been considered, but are moot in light of the withdrawal of the rejection and/or the new ground of rejection made below.

Rejection(s) under 35 U.S.C. § 102

10) Claims 25, 27, 28, 31 and 35-39 are rejected under 35 U.S.C. § 102(a) as being anticipated by Andreoni *et al.* (WO 99/49892A2, Original & English translation, already of record) as evidenced by Merle-Poitte (*Doctoral Thesis*. Universite de Nice, France, pages 1-132, 1995 - French Thesis and English translation of the front page, pages 9-11 and 26-48) and Bechetoille *et al.* (US 20050008623).

Andreoni *et al.* taught a process of delivering a *Klebsiella* membrane protein as a pharmaceutical composition to improve a mammal's immunity to an antigen or hapten, i.e., a biologically active substance that is associated with it (see abstract; and claims). The biologically active substance is a peptide, a polysaccharide, an oligosaccharide, or a nucleic acid, which is coupled covalently to the OmpA protein via an amino acid linker, i.e., attachment element, such as Cys, aspartic acid or ornithine (see Example 3; and claims 7 and 14-16). The OmpA protein is produced by extraction from an enterobacterial culture or by a recombinant process (see Examples 1 and 2; and claims 4 and 5). The amino acid sequence of the rP40 OmpA is depicted in pages 1 and 2 under 'Liste De Sequences', which meets the description of the amino acid sequence recited in the instant claims. The biologically active substance is a recombinant hybrid (i.e., chimeric) protein (see claim 17). That the prior art method involves the contacting of the biologically active substance coupled to rP40 with the mammal's antigen-presenting cells including dendritic cells is

inherent from the teachings of Andreoni *et al.* in light of the fact that rP40 OmpA coupled to the biologically active substance inherently and necessarily comes in contact with antigen-presenting cells *in vivo* in the mammal's body to whom the coupled rP40 has been delivered, wherein the coupled biologically active substance gets internalized. For example, Merle-Poitte taught that the P40 protein of *Klebsiella pneumoniae* has significant adjuvant activity and the capacity to bind to the membrane structure of antigen presenting cells or APC (i.e., dendritic cells, monocytes or B lymphocytes) (see page 3 of the translated document). Merle-Poitte disclosed the lympho-proliferation of lypmphatic cells by contacting the P40 with the inguinal lymphatic cells and T-lymphocytes. Merle-Poitte taught coupling the rP40 to a biologically active substance, such as, a peptide or an oligosaccharide. Most importantly, Merle-Poitte taught that associating an antigen with the P40 protein of *Klebsiella pneumoniae* increases the amount of antigens captured (i.e., internalized) by the APC. The resultant targeting of the APCs is taught to promote the antigen-cell interaction, improve the presentation of the antigen, and increase the immune response against the antigen. See third full paragraph on page 3; and part IV including subparts 4.3; 4; 4.1.2; 4.1.3; 4.2; 4.2.1; and 4.2.2 of the translated document.

That the 'antigen capturing' by the APC represents internalization is inherent from the prior art teaching in light of what is well known in the art. For instance, see section [0233] of Bechetoille *et al.*

Claims 25, 27, 28, 31 and 35-39 are anticipated by Andreoni *et al.* The reference of Merle-Poitte or Bechetoille *et al. et al.* is **not** used as a secondary reference in combination with the reference of Andreoni*et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Andreoni *et al.* with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

11) Claims 25, 27, 28, 31, 35, 36 and 39 are rejected under 35 U.S.C. § 102(b) as being anticipated by Binz *et al.* (WO 97/41888-A1, already of record - English translation provided) as evidenced by Pease *et al.* (US 2004/0014207 A1), Merle-Poitte (*Doctoral Thesis*. Universite de Nice, France, pages 1-132, 1995 - French Thesis and English translation of the front page, pages 9-11 and 26-48), and Bechetoille *et al.* (US 20050008623).

The page numbers indicated below refer to the page numbers in the translated document of Binz *et al.*

Binz *et al.* disclosed a method of injecting (i.e., delivering) into the popliteal lymph nodes of rabbits the recombinant P40 OmpA protein of *Klebsiella pneumoniae* chemically and covalently coupled to a biolologically active substance, such as, a bacterial oligosaccharide (i.e., antigen or hapten). The recombinant P40 OmpA protein of *Klebsiella pneumoniae* has the amino acid sequence of SEQ ID NO: 2 having a 9 amino acid leader peptide sequence of the tryptophan operon, Met Lys Ala Ile Phe Val Leu Asn Ala (see pages 36 and 37; pages 15 and 39; and Example 8). In this rejection, it should be noted that the prior art 9 amino acid leader peptide sequence of the tryptophan operon, Met Lys Ala Ile Phe Val Leu Asn Ala, corresponds to amino acid residues 1-9 of the instantly recited amino acid sequence of SEQ ID NO: 2 and the prior art amino acid sequence of SEQ ID NO: 2 corresponds to amino acid residues 10 through 344 of the instantly recited SEQ ID NO: 2. See the sequence search report attached to the Office Action mailed 09/08/04. The covalent coupling is accomplished via attachment elements, such as, ADH linkers (see page 13). The P40-oligosaccharide conjugate elicited high levels of IgG antibodies to the oligosaccharide (see Example 8). The prior art method, comprising the two instantly recited steps, inherently serves as a method of delivering the biologically active oligosaccharide coupled to the recombinant P40 OmpA protein of *Klebsiella pneumoniae* to antigen-presenting cells, including dendritic cells, because it is known in the art that dendritic APCs are present in the popliteal lymph nodes. For instance, see section [0127] of Pease *et al.*

That the prior art method involves the contacting of the biologically active substance coupled to rP40 with the rabbit's antigen-presenting cells including dendritic cells wherein it gets internalized is inherent from the teachings of Andreoni *et al.* in light of what is known in the art. For example, Merle-Poitte taught that the P40 protein of *Klebsiella pneumoniae* has significant adjuvant activity and the capacity to bind to the membrane structure of antigen presenting cells or APC (i.e., dendritic cells, monocytes or B lymphocytes) (see page 3 of the translated document). Merle-Poitte disclosed the lympho-proliferation of lypmphatic cells by contacting the P40 with the inguinal lymphatic cells and T-lymphocytes (i.e., APC or antigen-presenting cells). Merle-Poitte taught coupling the rP40 to a biologically active substance, such as, a peptide or an oligosaccharide. Most importantly, Merle-Poitte taught that associating an antigen with the P40 protein of *Klebsiella pneumoniae* increases the amount of antigens captured (i.e., internalized) by the APC. The resultant targeting of the APCs is taught to promote the antigen-cell interaction, improve the presentation of

the antigen, and increase the immune response against the antigen. See third full paragraph on page 3; and part IV including subparts 4.3; 4; 4.1.2; 4.1.3; 4.2; 4.2.1; and 4.2.2 of the translated document. That the 'antigen capturing' by the APC represents internalization is inherent from the prior art teaching in light of what is well known in the art. For instance, see section [0233] of Bechetoille *et al.*

Claims 25, 27, 28, 31, 35, 36 and 39 are anticipated by Binz *et al.* The reference of Pease *et al.*, Bechetoille *et al.* or Merle-Poitte is **not** used as a secondary reference in combination with Binz *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Binz *et al.* ('273) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Remarks

12) Claims 25, 27, 28, 31 and 35-39 stand rejected.

13) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The central Fax number for submission of amendments, responses and papers is (703) 872-9306.

14) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

15) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor,

Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER